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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,341	11/28/2000	Avi J. Ashkenazi	P1805R1	7279

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 01/30/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,341	ASHKENAZI ET AL.	
	Examin r	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *67-97* is/are pending in the application.

4a) Of the above claim(s) *92-94 and 97* is/are withdrawn from consideration.

5)☒ Claim(s) *69,71,72,74,75,77,78,80-88,90 and 91* is/are allowed.

6)☐ Claim(s) *67-68, 70, 73, 76, 79, 89 and 95-96* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 12/02/2003, is acknowledged.

2. Claims 67-97 are pending.

Newly submitted claim 97 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: because claim 97 is drawn to a method of using anti-APRIL antibody, however the elected invention is directed to the anti-APRIL antibody.
Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 97 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

3. Claims 92-94 and 97 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected invention.

4. Claims 67-91 and 95-96 are under examination as they read on an antibody that binds APRIL polypeptide and hybridoma thereof.

5. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) to the provisional applications 60/182,938, filed February 16, 2000 and 60/226,986, filed August 22, 2000.

6. The formal drawing submitted 12/02/03 is objected to because Fig 17F shows only part of the joints of CIA mice, Fig 9A depicts only letters without pictures and Fig 8A does not show any bands.

7. In view of the amendment filed on 12/02/2003, only the following rejections are remained.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> *The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

9. Claims 70, 73, 76, 79, 89 and 95-96 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody which specifically bind SEQ ID NO: 8 and the specific monoclonal antibody of 3C6.4.2, 5E11.1.2, 5G8.2.2 and 5E8.7.4 secreted by the PTA-1347, PTA-1346, PTA-1345 and PTA-1344, respectively, a chimeric and a humanized antibody thereof for blocking the APRIL binding to BCMA and to TACI, does not reasonably provide enablement for any monoclonal antibody which binds to "the same epitope as the epitope" to which the 3C6.4.2, 5E11.1.2, 5G8.2.2 and 5E8.7.4 monoclonal antibody produced by the hybridoma cell line deposited as ATCC accession number PTA-1347, PTA-1346, PTA-1345 and PTA-1344, respectively binds or an anti-APRIL monoclonal antibody that competitively inhibits the binding of

the 3C6.4.2/5E11.1.2 antibody secreted by the hybridoma deposited with ATCC as accession number PTA-1346/PTA-1346 to APRIL in claims 95-96. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, mailed 06/02/2003.

Applicant's arguments, filed 12/02/2003, have been fully considered, but have not been found convincing.

Applicant asserts that the specification as filed provides the proper guidance. Further, Applicant asserts that the application states that epitope binding properties can be determined, e.g., by a competitive inhibition binding assay (e.g., page 65, line 39 to page 66, line 8 of the specification). Based competitive assay using ELISA disclosed in example 8 and a binding assay useful for testing the blocking activity of anti-APRIL antibodies disclosed in example 9, Applicant concluded that one of ordinary skill in the art could easily determine whether other antibodies bound to the same epitope of any one of the specifically disclosed antibodies. Applicant concludes that the antibodies of amended claims 70, 73, 76, 79 and 89 are enabled.

Regarding applicant's argument that that the specification provides a working example and substantial guidance on how to identify polypeptides that have the recited activity, the examiner notes that in order to satisfy the U.S.C 112, 1st paragraph, the specification has to teach how to make and/or use the invention, not how to screen to identify the invention. Until the time when the epitope sequences to which the specific antibodies bind identity are found, then one skill in the art can make them then make antibody to those epitope sequences and screen for the specific activity. Thus it would require undue experimentation of the skilled artisan to determine the epitope sequences to which the specific antibodies bind and hence make the epitope sequences and then make antibodies to those sequences and then screen for the antibodies that would have the function of the specific activity. As stated previously, Van Regenmortel notes that 90% of antibodies raised against intact proteins do not react with any peptide fragment derived from the parent protein indicating that these antibodies are directed to discontinuous epitopes (see page 466, column 1 in particular). In addition Van Regenmortel states that the low success rate of antigenic prediction is due to the fact that predictions concern only continuous epitopes and it is unrealistic to reduce the complexity of epitopes that always possess conformational features to one-dimensional, liner peptide models (see page 467, column 2 in particular).

10. Claims 70, 73, 76, 79, 89 and 95-96 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention for the same reasons set forth in the previous Office Action, mailed 06/02/2003.

Applicant's arguments, filed 12/02/2003, have been fully considered, but have not been found convincing.

Applicant argues that amended claims 70, 73, 76 and 79 representatively describe an object having both structural and functional characteristics - - an antibody which has the functional characteristics of specifically binding to an APRIL polypeptide and an epitope recognized by an antibody specifically disclosed in the application.

While the instant claims indicate that the antibody specifically binds to an APRIL polypeptide and binds to the same epitope, still there is no described or art-recognized correlation or relationship between the structure of the invention, APRIL polypeptide and epitope recognized by an antibody and it's blocking ability to a TACI receptor or a BCMA receptor function, the feature deemed essential to the instant invention. Therefore, one of skill in the art would not envisage, based on the instant disclosure, the claimed antibodies that bind to an APRIL polypeptide and bind to the same epitope recognized by the specific antibody which retain the features essential to the instant invention.

Further, Applicant argues that the guidelines indicate that the need for a disclosure of a representative number is balanced against the skill and knowledge in the art. Fed. Reg. 66(4):1106, col. 3, lines 39-42. Applicant submits that the specification teaches and demonstrates that antibodies that bind to the epitopes described in this invention can easily be
Determined by performing competitive binding assays using a APRIL polypeptide and the
antibodies specifically disclosed and deposited (e.g., page 65, line 39 to page 66, line 8 and
Example 9 of the specification as filed). Applicant concluded that one of ordinary skill in the art would immediately recognize that applicants were in possession of the necessary common attributes or features of the elements possessed by the members of the genera.

The broad brush discussion of making and screening for epitopes that are recognized by the specific antibodies does not constitute a disclosure of a representative number of members. No such epitopes were made. Only the polypeptide specific antibodies secreted by the specific hybridoma are disclosed. The specification's general discussion of making and screening for those epitopes constitutes an invitation to experiment by trial and error. Such does not constitute an adequate written description for the claimed variants.

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e2) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) do not apply to the examination of this application as the application being examined was not (1) filed on or after November 29, 2000, or (2) voluntarily published under 35 U.S.C. 122(b). Therefore, this application is examined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

12. Claims 67-68 and 89 are rejected under 35 U.S.C. 102(b) as being anticipated by WO/9900518 (IDS Ref. # 6, filed 3/17/03), as is evidenced by the specification on page 10, lines 12-15 and Bost et al for the same reasons set forth in the previous Office Action, mailed 06/02/2003.

Applicant's arguments, filed 12/02/2003, have been fully considered, but have not been found convincing.

Applicant submits that page 5 of the `518 publication refers to refers to antibodies that specifically bind to an epitope of TNF-gamma. No polyclonal antibodies were made or tested in the `518 publication. No specific monoclonal antibodies were made or tested in the `518 publication. Furthermore, no receptors were identified for the TNF-gamma protein in the `518 publication.

Contrary to applicant assertions the `518 publication teaches "An antibody which specifically binds to at least one epitope encoded by TNF-gamma is provided herein. The antibody is polyclonal or monoclonal. The epitope comprises an amino acid sequence having at least 35% identity to an amino acid sequence selected from the group consisting of SEQUENCE ID NO 2, SEQUENCE ID NO 3 and fragments thereof".

Applicant contends that to anticipate a claim, the reference must teach each and every element of the claim.MPEP 2131. Applicant argues that nowhere does the `518 publication specifically teach monoclonal antibodies that block TACI or BCMA binding to APRIL. Applicant concluded that recitation of those elements are missing from the `518 publication.
Regarding "inherent property" and "Applicant's burden" to show that the reference antibody does not bind to SEQ ID NO:2, Applicant contends that the Examiner is mistaken for the following reasons:

First, an antibody that blocks TACI and/or BCMA binding to APRIL would not have been envisaged by one of skill in the art prior to this invention. Applicant argues that to establish inherency, the extrinsic evidence must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. MPEP 2112. Applicants believe that the instant application is the first identification of any receptor for APRIL. The present application describes TACI and
BCMA as receptors for APRIL and the discovery that TACI and BCMA can be activated directly through APRIL binding (e.g., Example 4 of the specification).

Second, the claimed blocking ability of the anti-APRIL antibodies of claims 67-68 is not an "inherent property" of all antibodies that bind APRIL. In relying upon the theory of inherency, the Examiner must provide "a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art." MPEP 2112. An antibody that is reactive against a part of APRIL that does not bind TACI or BCMA may not block the binding of TACI or BCMA to APRIL. The `518 publication, without providing, specific antibodies, only generally refers to antibodies that bind APRIL. Applicant argues that the `518 publication cannot distinguish between antibodies that block APRIL binding to TACI and/or BCMA because it does not identify any receptor for APRIL. Applicant concluded that the Examiner has not shown that the alleged "inherent property" necessarily flows from the teachings of the `518 publication.

Third, claims 67-68 and relevant parts of claim 89 depending therefrom are not directed to all antibodies that bind APRIL, rather they are directed to a specific set of monoclonal antibodies against APRIL that have special properties and characteristics that are not described in the `518 publication and are not of the same scope as the antibodies described in the `518 publication. Thus, a rejection based on inherent anticipation is not proper.

Finally, contrary to the Examiner's assertions, applicants have no burden to show that the antibodies of the `518 publication do not bind to APRIL because (1) the `518 publication does not inherently anticipate claims 67-68 and 89 for the above reasons and because (2) antibodies that generally bind APRIL are not the subject matter of the claims at issue

In contrast to applicant's assertions; when a claim recites using an old composition or structure (e.g. A monoclonal anti-APRIL antibody) is directed to a result or property of that composition or structure (e.g. blocks binding of APRIL polypeptide to a TACI receptor or a BCMA receptor), then the claim is anticipated. See MPEP 2112.02.

While the prior art disclosure may be silent as to the "blocks binding of APRIL polypeptide to a TACI receptor or a BCMA receptor" per se; the instant claims merely recite newly discovered results of "blocks binding of APRIL polypeptide to a TACI receptor or a BCMA receptor" of a known Anti-APRIL antibody. A recitation of the intended use of the claimed invention (blocks binding of APRIL polypeptide to a TACI receptor or a BCMA receptor) must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. For example in Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999); the following was noted. "Artisans of ordinary skill may not recognize the inherent characteristics or functioning of the prior art. However, the discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably

new to the discoverer. " The Court further held that "this same reasoning holds true when it is not a property but an ingredient which is inherently contained in the prior art". See MPEP 2112.02. Also, see Bristol-Myers Squibb Co. v. Ben Venue Laboratories, Inc. 58 USPQ2d 1508 (CA FC 2001); Ex parte Novitski 26 USPQ 1389 (BPAI 1993); Mehl/Biophile International Corp. V. Milgraum, 52 USPQ2d 1303 (Fed. Cir. 1999); Atlas Powder Co. V. IRECO, 51 USPQ2d 1943 (Fed. Cir. 1999).

Applicant argued that the reference is silent about all of the claimed properties and that the reference antibodies that generally bind APRIL are not the subject matter of the claims at hand, but had not provided any objective evidence to support these assertions. Whether the rejection is based on "inherence" under 35 U.S.C. § 102 or prima facie obviousness under 35 U.S.C. § 103, jointly or alternatively, the burden of proof is the same and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. Examiner properly shifted burden to applicant to establish, through objective evidence, that monoclonal antibodiy of invention differ in unobvious manner from those of the prior art references. Ex parte Phillips, 28 USPQ2d 1302 (BPAI 1993). Here, applicant has not provided any objective evidence to support the difference between the prior art and instant antibodies. The record does not contain sufficient objective evidence that the referenced antibodies differ in any significant manner from that claimed.

13. Claims 67 and 68 sand rejected under 35 U.S.C. 102(e2) as being anticipated by U.S. Patent No.6,440,694, as is evidenced by the specification on page 10, lines 12-15 for the same reasons set forth in the previous Office Action, mailed 06/02/2003.

Applicant's arguments, filed 12/02/2003, have been fully considered, but have not been found convincing.

Applicant argues the same as under 35 U.S.C. 102(b) above. Therefore, the Examiner rebuttal is the same as above.

14. Claims 69, 71-72, 74-75, 77-78, 80-88 and 90-91 are allowable.

15. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (571) 272-0845. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (571) 272-0841. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

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January 26, 2004

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